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Intravenous catheter infections associated with bacteraemia: a 2-year study in a University Hospital

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ABSTRACT

The aim of this retrospective study was to assess the incidence and aetiology of central and peripheral venous catheter (C/PVC) infections during a 2-year period (1999–2000) and to determine the susceptibility of isolated microorganisms to various antimicrobial agents. Catheter tips were processed using the semiquantitative method and blood cultures were performed with the BacT/Alert automated system. Antibiotic susceptibilities were performed by disk agar diffusion and MICs were determined by Etest, according to NCCLS standards. During the study period, samples from 1039 C/PVC infections were evaluated, yielding 384 (37.0%) positive cultures. Blood cultures were also available from 274 patients, of which 155 (56.6%) yielded the same microorganism as from the catheter. No bloodstream infections were detected in 104 C/PVC-positive cases. Methicillin-resistant coagulase-negative staphylococci were the most frequent isolates, followed by Gram-negative bacteria, especially *Pseudomonas aeruginosa*. Resistance to glycopeptides among staphylococci and enterococci was not detected, whereas 60% of Gram-negative bacilli were resistant to β-lactams.

Keywords Catheter-related bloodstream infections, antibiotic susceptibility

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INTRODUCTION

The use of intravascular catheters for vascular access and haemodynamic monitoring has become a central part of modern medicine [1]. Infections with significant morbidity and mortality are the predominant complications associated with the use of these devices [1,2]. Intravenous catheters are the commonest cause of hospital-acquired bloodstream infections [3]. A steady rise in the incidence of intravascular catheter-associated infections has been observed, reflecting the increasing role of catheters in patient management. This has occurred despite emerging evidence-based measures to reduce infection complications [1,3].

The most recent guidelines of the Centers for Disease Control and Prevention define a colonised catheter as one yielding growth of at least 15 CFU by semiquantitative culture, or $> 10^3$ CFU by quantitative culture from a proximal or distal catheter without clinical signs of infection [4]. Catheter-related bloodstream infection (CRBSI) is defined as the isolation of the same organism from blood culture as from a semiquantitative or quantitative catheter culture in the presence of systemic signs of bloodstream infection and no other apparent source of infection [1,4]. Catheter infection without bloodstream infection requires systemic evidence of infection, the presence of at least 15 CFU on the catheter tip, and absence of bloodstream infection with the organism found on the catheter tip [1,4].

One major aspect of catheter-related sepsis that needs to be taken into account in any preventive strategy is the source of the microorganisms. Bacteria can gain access to intravascular catheters by migration from skin at the time of insertion, via the internal lumen of the device, or by spread from the skin insertion site along the external surface [1,4,5]. Two other sources, which are considered to be relatively minor contributors to sepsis, are haematogenous spread from other body sites or from a contaminated infusion [1,3–5].

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Various attempts have been made to quantify the burden of disease caused by intravascular device-associated infection. The objective of this retrospective study was to determine the incidence of catheter-related infections, as well as the responsible microorganisms, in a tertiary care teaching hospital. In addition, the antibiotic susceptibility profiles during a 2-year period are reported.

METHODS

Setting

The University Hospital of Patras is a 750-bed tertiary care teaching hospital receiving patients from south-west Greece. It includes departments of internal medicine, paediatrics, obstetrics, cardiology, pulmonary diseases, infectious diseases, haematology, renal and dermatology, as well as surgery wards (general, orthopaedic, and neurosurgery), and intensive care units (ICUs) for adults and neonates. During 1999 and 2000, the numbers of patients admitted were 52 143 and 54 019, respectively.

Isolates

During 1999 and 2000, 530 and 509 central and peripheral venous catheter (C/PVC) tips were received for culture. Specimens were collected according to clinical signs of catheter exit-site infection or device-related bloodstream infection in the absence of other sources [1,3,4]. Patients were hospitalised in the department of internal medicine, the renal unit, general surgery, orthopaedics, or the two ICUs. Blood cultures were also taken from the central venous catheter and/or from a peripheral venepuncture. Catheter tips were cultured only when infection was suspected, and were processed using the semiquantitative method of Maki *et al.* [6]; using flamed forceps, the catheter segment was rolled back and forth at least four times on a 5% blood agar plate and incubated for 24–48 h at 37 °C. Blood cultures were incubated using the BacT/Alert automated system (bioMérieux, Durham, NC, USA). Blood culture bottles giving a positive reading were subcultured on to MacConkey and 5% blood agar plates. Following incubation, isolates were identified to the species level using standard biochemical methods.

Antibiotic susceptibility testing

Antibiotic susceptibility testing was performed by agar disk diffusion using antibiotic disks (Becton Dickinson, Cockeysville, MD, USA), selected according to the microorganism isolated [7]. Etests (AB Biokisk, Solna, Sweden) were used to determine MICs [8]. Results by both methods were evaluated according to NCCLS criteria [7,8].

Definitions

Central or peripheral catheter infection without bloodstream infection (C/PVC-BSI) was defined as systemic evidence of infection, with the presence of at least 15 CFU on the catheter tip, but an absence of bacteraemia with the organism isolated from the catheter. CRBSI required the presence of bacteraemia, with the organism isolated from the catheter tip present in at least two additional peripheral blood samples besides those obtained through the catheter [1,3,4,6].

Statistical analysis

All comparisons were unpaired and determined by the Students' *t*-test with equal or unequal variance. All values are expressed as a percentage of the group from which they were derived, with $p < 0.05$ considered to be significant.

RESULTS

Of 1039 catheter tip cultures during the study period (530 in 1999 and 509 in 2000), 384 (37.0%) were positive. No blood cultures were available from 110 patients with positive C/PVC samples, and these patients were excluded from the study. Of the remaining 274 cases, 104 (37.9%), 45 in 1999 and 59 in 2000, were C/PVC-BSI, while 155 (56.6%), 69 in 1999 and 86 in 2000, involved CRBSI. Fifteen more cases (5.5%) were associated with bacteraemia caused by a different organism to that isolated from the catheter tip.

Among the CRBSI group, 104 (67.1%) Gram-positive bacteria were identified. Coagulase-negative staphylococci (CNS) were recovered from 92 patients (59.4%). Gram-negative bacteria were identified from 43 (27.8%) patients, with a predominance of *Pseudomonas aeruginosa* (19 patients; 12.3%). Fungi were isolated from eight patients (5.1%) during the study period (three isolates in 1999 vs. five in 2000) (Table 1).

Among the 104 patients with C/PVC-BSI, Gram-positive bacteria were isolated from 63 (60.6%) patients with CNS being the predominant organisms ($n = 50$; 48%). Thirty-three (31.7%) Gram-negative bacteria and eight (7.7%) fungi were also isolated (one isolate in 1999 vs. seven in 2000) (Table 1). There was no significant difference in the isolation of Gram-positive or Gram-negative bacteria between the two groups (CRBSI and C/PVC-BSI) (p 0.73 for Gram-positive, p 0.65 for Gram-negative; p 0.72 for fungi).

Most CNS were isolated from patients entering the general surgery and the internal medicine departments (Table 1). *P. aeruginosa* was isolated mainly from the adult ICU, while half of the other Gram-negative bacilli were recovered from catheter-related infections at the department of general surgery (Table 1). Among the CNS isolated during 1999 and 2000 from patients with catheter-related infection, 73% and 64%,

Table 1. Microorganisms isolated from intravenous catheter-related infections of patients located in different hospital wards[a]

Organisms isolated	CRBSI					C/PVC-BSI				
	GS	IM	ICUa	ICUn	Total (%)	GS	IM	ICUa	ICUn	Total (%)
CNS	37	34	14	7	92 (59.4)	16	17	16	1	50 (48)
Staphylococcus aureus	1	7	–	–	8 (5.1)	1	1	–	–	2 (2)
Enterococci	1	3	–	–	4 (2.6)	4	3	–	–	7 (6.7)
Streptococci	–	–	–	–	–	1	3	–	–	4 (3.9)
Pseudomonas aeruginosa	7	3	9	–	19 (12.3)	4	3	13	–	20 (19.2)
Other Gram-negatives[b]	15	3	4	2	24 (15.5)	3	5	4	1	13 (12.5)
Fungi	3	4	–	1	8 (5.1)	2	3	2	1	8 (7.7)
Total (%)	64 (41.3)	54 (34.8)	27 (17.4)	10 (6.5)	155 (100)	31 (29.8)	35 (33.6)	35 (33.6)	3 (3)	104 (100)

[a]Hospital wards: GS: General Surgery; IM: Internal Medicine; ICUa: Intensive Care Unit for adults; ICUn: Intensive Care Unit for neonates.
[b]Gram-negative bacilli, other than *P. aeruginosa*.
CNS, coagulase-negative staphylococci; CRBSI, catheter-related bloodstream infection; C/PVC-BSI, central or peripheral catheter infection without bloodstream infection.

respectively, were resistant to oxacillin. All staphylococci were sensitive to netilmicin and glycopeptides (vancomycin and teicoplanin) (Fig. 1a,b). No vancomycin-resistant *Enterococcus* spp. were identified.

Gram-negative bacteria showed high levels of resistance to β-lactam antibiotics and 5% resistance to imipenem (Fig. 1c). *P. aeruginosa* showed high resistance rates to anti-pseudomonal penicillins- and lower resistance rates to netilmicin and aztreonam (Fig. 1d), while three isolates were resistant to all antimicrobial agents tested.

DISCUSSION

In the USA, more than half of all hospital inpatients receive an intravascular catheter, whereas in Europe the incidence is 63% [1]. In 1998, over 150 million catheters were used in the USA, and the number of cases of bacteraemia or fungaemia associated with intravascular catheters rose to over 400 000 cases annually [2]. Most of these were associated with central vein catheters. If there is an attributable mortality of 20%, then 80 000 deaths are associated with intravascular catheter sepsis annually in the USA alone [2]. Compared to peripheral or arterial catheters, central venous catheters are associated with a higher rate of line-associated bacteraemia (4–14%) [1]. The pathogenesis of intravascular catheter-associated infection is complex and begins with attachment and colonisation of either the outer or inner surface of the catheter by the infecting microorganism. The outer surface of the catheter may become colonised with organisms originating from skin, either by direct extension from a contiguous infectious process, or by haematogenous seeding. Alternatively, the inner surface of the catheter may become colonised by the introduction of organisms through the catheter hub [1,4].

Once colonisation occurs, the opportunity for development of infection is present. Although the relationship between the level of colonisation and infection is not straightforward, there is good evidence that the presence of local and bloodstream infection is related to the number of microorganisms present on the catheter, as detected by semiquantitative roll-plate and sonication methods [6,9]. In our clinical microbiology laboratory, the semiquantitative technique was applied to identify infection of C/PVCs. Of 1039 catheter tips, 384 (36.9%) were positive during the study period. One hundred and ten samples were excluded from the study because of incomplete evidence of catheter-related infection. There was no significant difference in the total number of catheter-related infections between the years 1999 and 2000. However, isolates of *Candida* spp. increased from four to 12.

Many studies suggest that the risk of CRBSI is highly associated with age, site of insertion, repeated catheterisation, duration of catheterisation, experience of the person inserting the catheter, absence of antibiotic therapy and underlying disease (i.e., haematological malignancies, neutropenia, solid tumours, diabetes, haemodialysis, use of corticosteroids and patients treated in ICUs) [3]. In our study group, 155 (56.6% of those who could be evaluated) had CRBSI, whereas a different microorganism was isolated in 15 (3.9%) cases. Pelletier *et al.* reported that 17.6% of bacteraemia cases were associated with organisms different from those isolated from the catheter tip, and that an unrelated bacteraemia is most likely to develop in ICU patients [3].

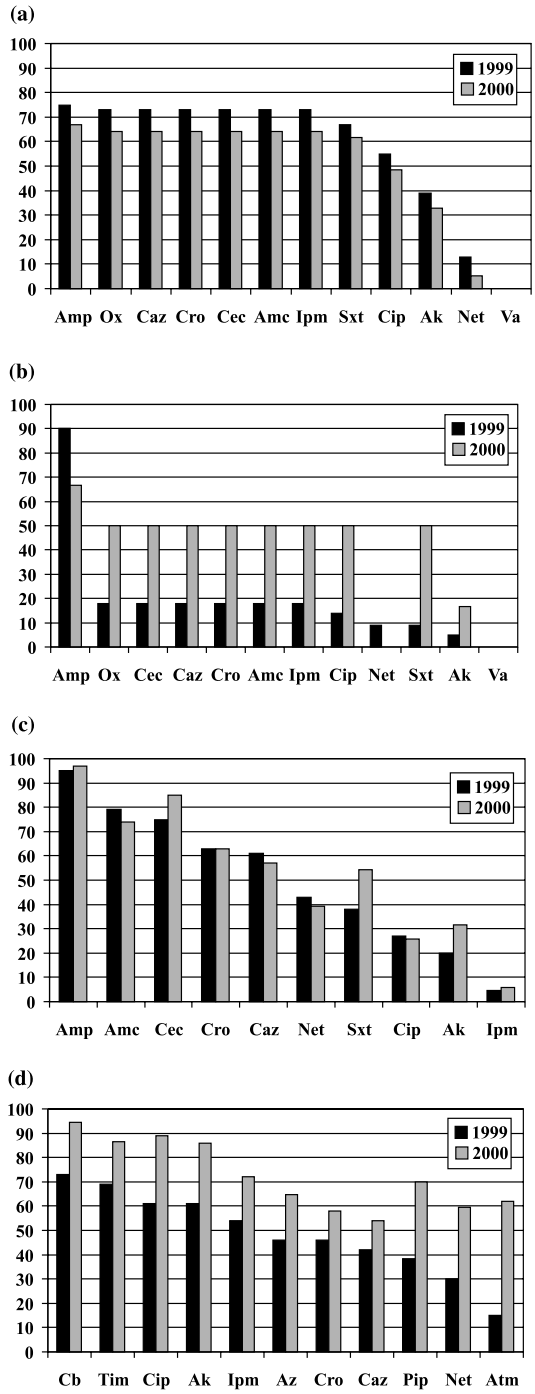

Fig. 1. Antibiotic resistance patterns of: (a) coagulase-negative staphylococci, (b) *Staphylococcus aureus*, (c) Gram-negative bacilli other than *Pseudomonas aeruginosa,* and (d) *P. aeruginosa*. Ampicillin (Amp), oxacillin (Ox), cefaclor (Cec), ceftazidime (Caz), ceftriaxone (Cro), amoxycillin with clavulanic acid (Amc), imipenem (Ipm), ciprofloxacin (Cip), netilmicin (Net), amikacin (Ak), sulphamethoxazole-trimethoprim (Sxt), vancomycin (Va), carbenicillin (Cb), ticarcillin with clavulanic acid (Tim), azlocillin (Az), piperacillin (Pip), aztreonam (Atm).

However, the present study did not identify an association between these cases and hospitalisation on a particular ward. In addition, the results showed no significant differences in the isolation of Gram-negative or Gram-positive bacteria associated with C/PVC-BSI, as compared with CRBSI.

In a study performed during a 3-year period in the surgery ward of the University Hospital of Charlottesville, Gram-negative organisms predominated among patients with CRBSI [3]. As in the present study, the most frequent isolates were CNS, and especially methicillin-resistant *Staphylococcus epidermidis* strains (Fig. 1a) [3]. *S. epidermidis*, the commonest species of the normal human skin microflora, is the predominant organism isolated from medical devices [10,11]. The adherence of these bacteria to surfaces, the secretion of an extracellular polysaccharide (slime), and the formation of biofilm protects the bacteria from antibiotics and the host immune system [12–14]. Methicillin resistance, which was identified in most of our isolates, is associated with more virulent strains. It has been shown that *S. epidermidis* variants lacking *mecA* expression show a strongly reduced adherence capacity, offering further evidence that *mecA*-positive staphylococci are associated more often with infectivity than colonisation among patients [15,16]. In a study performed in our laboratory, the spread of certain clones was identified among methicillin-resistant CNS isolated from catheter infections [17].

P. aeruginosa was the predominant Gram-negative species isolated, especially from the ICU patients, and the rate of isolation rose during 2000. Multiresistant strains were also identified, again with increasing incidence in 2000 (Fig. 1d). Even though the incidence of CRBSI caused by Gram-negative bacilli is reported to be lower than that of Gram-positive bacteria [4,18], *P. aeruginosa,* as well as other multiresistant Gram-negative bacteria (*Escherichia coli, Acinetobacter* spp., *Klebsiella pneumonia*), has been shown to cause intravascular catheter-related infections in several institutions [19–21], as well as in our own hospital. *P. aeruginosa* strains are characterised by their ability to produce an extracellular polysaccharide (alginate) which enhances bacterial adhesion and survival on catheters or other biomedical materials [19].

An increasing incidence of intravascular catheter-associated infections has been observed worldwide, reflecting the rise in invasive

procedures. The use of the less expensive semi-quantitative method for processing catheter tips in combination with blood cultures may improve diagnosis of CRBSI. In the present study, methicillin-resistant CNS were the predominant species isolated, followed by *P. aeruginosa*. The isolation of these resistant organisms highlights the need for new preventative and therapeutic measures.

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